

REMARKS

① Following the suggestion of the Examiner, the specification has been amended to clarify that the term "i.m." stands for "intramuscular." The amendment merely serves to clarify the previous language, and does not add new matter. The newly added claims are fully supported in the specification, e.g., in claims 2, 4 and 5.

② Applicants do not understand the rejection under 35 USC 112, first paragraph. The Examiner admits that the specification is enabling for the recited dosage of a generic gestagen. Therefore, the specification is also enabling for any of the species of gestagens recited in claims 15-17. Support that the genus of "gestagens" includes the species of gestagens recited in claims 13 and 14 is found in the specification, e.g., at page 6, lines 3-10. The Examiner has provided no evidence or sound scientific reasons to doubt applicants' assertion that any of the species encompassed by the genus of gestagens can be administered in the dosage disclosed for the genus as a whole.

③ As for the obviousness rejection, it is noted at the outset that applicants were the first to recognize that the administration of an androgen to treat a testosterone insufficiency can be associated with the development of a BPH or a prostate cancer, and that the administration of a second agent (e.g., a gestagen), in combination with the androgen, is useful for prophylaxis of such a BPH or a prostate cancer. The instant invention is not rendered obvious by the cited references, at least because they do not, taken individually or in combination, recite a method which involves administration of such a combination of agents, or a method which simultaneously treats a testosterone insufficiency and provides prophylaxis for a BPH or a prostate cancer.

* The primary reference cited, Hesch, does not suggest or disclose a combined treatment for a testosterone deficiency, comprising the administration of an androgen plus another agent, such as a gestagen (as the Examiner admits in the Office Action). Hesch may recognize that treatment with an androgen can, under some circumstances, lead to certain undesirable side effects, such as atherosclerosis, but it solves the problem by modifying the structure of the androgen to contain substituents with radical trapping properties (see, e.g., col. 3, lines 24-38), rather than by co-administering it with a second agent. If anything, the fact that Hesch solves the problem by

modifying the androgen, rather by co-administering it with a second agent, suggests against the method recited in the instant claims and motivates against the invention which recites a coadministration of agents.

★ *argue individual Ref.* The secondary reference, Neri, does not remedy the deficiencies of Hesch. While Neri may suggest treating an already existing BPH with a gestagen, it also does not suggest or disclose co-administration of anything else, just like Hesch. Moreover, there is no suggestion such an agent can be used for prophylaxis. The reference does not suggest or disclose that a gestagen is administered in combination with an androgen, or that a testosterone deficiency can be treated simultaneously with prophylaxis of a BPH or a prostate cancer.

★ *then both Refs. together unpredictable on when undesired side effects when co-admin.* Even if Neri had suggested administering a gestagen for prophylaxis of BPH (which is not admitted), and Hesch had disclosed administering an androgen for such prophylaxis (which is also not admitted), these suggestions taken together would not have provided motivation to administer the two agents in combination. The effects of the administration of hormones, individually or in combination, is notoriously difficult to predict, particularly in view of the complex interactions, feed-back mechanisms, and other physiological phenomena that occur among hormones in the body. It is not clear from the prior art that the co-administration would, e.g., not cancel each other out, or even create undesired side effects. The uncertainties about the effect of, e.g., androgens is illustrated by the various, sometimes contradictory, theories presented in the references of record. The Examiner has not satisfied her burden to show that the prior art motivates co-administration of the two agents for any purpose, let alone for beneficial results.

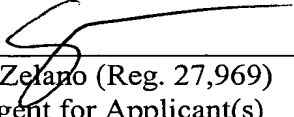
★ Absent motivation for a skilled worker to combine the disclosures of Hesch and Neri, with the requisite reasonable expectation of success, the references do not render the claimed invention obvious. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991).

The additional references cited in the Office Action for their disclosures of particular synthetic androgens, or for dosage forms, do not remedy the deficiencies of Hesch and Neri, and therefore do not render the claimed invention obvious.

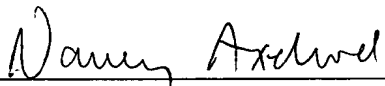
In view of these amendments and arguments, the application is believed to be in condition for allowance, which action is respectfully requested.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please replace the last paragraph on page 5 with the following paragraph:

It has proven advantageous that the dosage of the androgen, for example of testosterone undecanoate, is 250 to 1500 mg i.m. (intramuscular) every 4 to 14 weeks.
